

PHILIP MORRIS U. S. A.

INTER - OFFICE CORRESPONDENCE

Richmond, Virginia

To: Dr. C. K. Ellis

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From: A. H. Warfield

Subject: Abstract of TSNA Program Presentation at the 3rd Quarter Planning Meeting

The program objective is to prepare model cigarettes with reduced delivery of MS TSNA. Organic solvent extracts of oriental filler were prepared and evaluated for inhibition of pyrosynthesis. There was no consistent reduction due to these extracts. A large scale SC CO<sub>2</sub> extract of oriental filler was prepared. This extract will be fractionated during 4th quarter, 1990, and the fractions tested for reduction of MS TSNA.

Pseudo-oxynicotine (PsON) and N-methylmyosmine (NMM) are potential precursors of MS NNK. Successful development of two methods for analysis of PsON was achieved. PsON added to a filler was detected in an extract by reduction followed by GC/MSD, or by direct GC/NPD or GC/MSD. Evidence for the presence of PsON was detected in several untreated fillers. In 4th quarter, 1990, selected ion monitoring will be evaluated for MSD, and the PsON method development will be completed. In 1991 methods will be developed to determine PsON in smoke. An attempt was made to remove MS NNK precursors by washing filler with aqueous solutions of various salts, acids, and bases. Water alone resulted in 30% reduction in NNK (without dry weight loss correction), and only ammonia and HCl (1-2N) provided any further reduction, but the best that could be achieved was 47%.

Two types of alkali-releasable bound nicotines have been determined to exist in filler, and these may be precursors of MS NNK. Water-soluble (Nic-X) and water-insoluble (Nic-Y) bound nicotines were analyzed in burley, bright and oriental fillers and base webs made from these fillers. Nic-Y levels from the three fillers paralleled the levels of MS NNK found when the corresponding cigarettes were smoked: Bu>Br>Or. Enzymes were successfully used to cleave Nic-Y so that it could be made water soluble for evaluation and identification. In 4th quarter the enzyme digestion method will be optimized, followed by isolation of Nic-Y in soluble form. Nic-X was found to consist of two different materials differing in molecular weight: one is >4000 D, and the other is <4000 D. Evaluation of Nic-X and Nic-Y as precursors of MS NNK will be done in 4th quarter 1990. If a relationship is demonstrated, attempts will be made in 1991 to study the chemistry of Nic-X and Nic-Y.

To provide filler for a low-TSNA laboratory model cigarette, a blend of bright, burley and oriental fillers was extracted using our 95% ethanol process. Preformed TSNA, nicotine, and minor alkaloids were all reduced by 90% or better relative to the unextracted control. MS TSNA were reduced by 80% for NNN and NAT, and 60% for NNK. During 4th quarter, 1990, a low-TSNA BCR-RL will be developed for use in the low-TSNA laboratory model.

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To explore the use of SCFE for removal of minor alkaloids from tobacco, a series of experiments was conducted to evaluate the use of triethylamine (TEA) as a cosolvent for  $\text{CO}_2$ . Most of the experiments were carried out using hexane as a model for SC  $\text{CO}_2$ . It was demonstrated that 5% ethanol/hexane containing 3% TEA can be used to reduce nornicotine by 60% if a cation exchange scrubber is used to provide a controlled removal of bases from the recycling solvent stream. Plans for 4th quarter call for use of a TEA salt to localize the effect of TEA and eliminate the need to provide ion exchange capacity for it in the scrubber. Further interaction with other Research Directorate divisions is planned in 1991 to further study the removal of minor alkaloids by SCFE.

CC: R. Kinser  
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*A. L. Warfield*

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